EXHIBIT C

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Record 1 of 8

Recruiting

Psilocybin-Assisted Therapy in Treatment-Resistant Depression

ClinicalTrials.gov ID NCT06303739

Sponsor University of North Carolina, Chapel Hill

Information provided by University of North Carolina, Chapel Hill (Responsible Party)

Last Update Posted 2024-07-23

Study Details Tab

Feedback

Study Overview

Brief Summary

The goal of this clinical trial is to test how well psilocybin-assisted therapy works in treating people with depression. The main questions this study aims to answer are:

- Does psilocybin with assisted therapy help improve symptoms for people with depression?
- How long do the effects of this treatment last?

Participants will:

- Take part in a couple of screening and preparation visits.
- Be given psilocybin in one or two treatment sessions.
- Attend a series of follow-up sessions over the following year.
- Complete forms and surveys to test how their symptoms have changed and what they thought of their experience.

Researchers will also compare whether one treatment or two treatments help improve symptoms more for participants.

Detailed Description

Major depressive disorder (MDD) ranks fourth in global disease burden and has significant morbidity, mortality, societal and financial costs. However, few adequate and effective treatments exist with 60% of MDD patients not responding sufficiently to an initial oral antidepressant treatment. These patients who experience treatment resistant depression (TRD), defined as an intolerance or lack of response to two antidepressants of different classes, have limited treatment options beyond the antidepressant treatments that often yield insufficient results or relapse. Psilocybin, a novel treatment, has been found to relieve symptoms of TRD, but there are limited studies on specific dosing and long term treatment follow-up. In this study, the investigators will look closer at the effectiveness of one treatment with psilocybin versus two treatments with psilocybin, as well as the long term effectiveness over the first 12 months after treatment.

Official Title

Induction Protocol for Psilocybin-Assisted Therapy in Treatment-Resistant Depression (TRD): A Pilot Study

Conditions

Refractory Depression | Treatment Resistant Depression

Intervention / Treatment

- Drug: psilocybin

Other Study ID Numbers

- 22-1421

Study Start (Actual)

2024-04-19

Primary Completion (Estimated)

2025-09

Study Completion (Estimated)

2026-09

Enrollment (Estimated)

20

Study Type

Interventional

Phase

Phase 3

Resource links provided by the National Library of Medicine

MedlinePlus Genetics (https://medlineplus.gov/genetics/) related topics: Depression (https://medlineplus.gov/genetics/condition/depression)

FDA Drug and Device Resources (https://clinicaltrials.gov/fda-links)

Contacts and Locations

This section provides contact details for people who can answer questions about joining this study, and information on where this study is taking place.

To learn more, please see the Contacts and Locations section in How to Read a Study Record (https://clinicaltrials.gov/study-basics/how-to-read-study-record#contacts-and-locations).

Study Contact

Name: Brittania Ricketts
Phone Number:

Study Contact Backup

Name: Robert K McClure, MD
Phone Number:
9199286381

9849741004
Email: PilotPAT_study@med.unc.edu

Email: robert_mcclure@med.unc.edu

This study has 1 location

United States

North Carolina Locations

Chapel Hill, North Carolina, United States, 27514

Recruiting
UNC Chapel Hill Medical Center
Contact: Brittania Ricketts, BA
Principal Investigator: Robert K McClure, MD
Sub-Investigator: Amanda Tow, MD, PhD
Sub-Investigator: Lindley Reynolds, MSW

Participation Criteria

Researchers look for people who fit a certain description, called eligibility criteria. Some examples of these criteria are a person's general health condition or prior treatments.

For general information about clinical research, read Learn About Studies (https://clinicaltrials.gov/study-basics/learn-about-studies).

Eligibility Criteria

Description

Inclusion Criteria:

- Provision of signed and dated informed consent form.
- Willingness to comply with all study procedures and availability for the study.
- Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-V) diagnosis of major depressive disorder.
- Currently experiencing a major depressive episode, lasting at least 3 months
- Failure to respond or inability to tolerate at least 2 guideline-concordant pharmacological treatments from different pharmacologic classes during the current major depressive episode
- Good health evidenced by medical history and routine lab tests
- No central nervous system (CNS) or neurocognitive impairment
- Ability to take oral medication and to follow to the psilocybin-assisted therapy protocol
- Identified support person to accompany patient home after dosing
- Use of effective contraception throughout the study by those with child-bearing potential
- Use of condoms or other effective contraceptive methods by males with reproductive potential
- Fully vaccinated and up to date on vaccination against COVID-19, as defined by Center for Disease Control guidelines
- Following Lifestyle Considerations throughout study (no nicotine containing products in clinical unit, refrain from operating heavy machinery for the duration of treatment day, no more than two servings 8 hours prior to treatment, no psychoactive drugs 72 hours before treatment, refrain from consuming foods that would interfere with drug absorption, minimize interaction with household immunocompromised contacts)

Exclusion Criteria:

- Family history (first- or second-degree relatives) or diagnosis of bipolar disorder with psychotic features, schizophrenia, schizoaffective disorder, hallucinogen-induced psychosis, anti-social personality disorder, or other psychotic disorder.
- Borderline personality disorder, defined by DSM-V criteria, that in the judgement of the Investigator is likely to complicate the assessment of clinical response to study treatments or limits the patient's ability to comply with study procedures.
- Alcohol or other substance use disorder (except tobacco/nicotine) that has been active within the 6 months prior to enrollment.
- Recent use (within past 6 months) of esketamine, ketamine or classic hallucinogens (psilocybin-containing mushrooms or LSD) or use of psychedelics more than 10 times in lifetime.
- Participants with active suicidal ideation or plan with a Columbia Suicide Severity Rating Scale (C-SSRS) score greater than or equal to 4.

- Current active self-injurious behavior, requiring medical attention or per investigator discretion.
- Diagnosis of Obsessive-compulsive disorder or post-traumatic stress disorder.
- Within 72 hours of psilocybin administration, use of nicotine, alcohol, or other controlled substances.
- Current delirium, dementia, amnestic disorder, or other cognitive disorders.
- Any current or past medical or neurological illness (including chronic pain syndromes and/or history of cerebrovascular event (excluding migraine)) that, in the opinion of the investigator, may confound the interpretation of study assessments
- Known allergic reactions to components of psilocybin.
- Medically instability at screening, including hepatic, renal, circulatory, cardiac (arrhythmia, uncontrolled hypertension, systolic BP > 140 mmHg or diastolic BP > 90 mmHg, abnormal QTc), pulmonary or CNS (seizure disorder or treatment with antiepileptic drugs) impairment.
- Current pregnancy or lactation.
- Febrile illness in last 3 weeks.
- Current use or use within 4 weeks of psilocybin administration of Monoamine oxidase inhibitors (MAOIs), alcohol dehydrogenase inhibitors and antipsychotics (concomitant medications will be allowed per investigator discretion).
- Current treatment with buproprion greater than 300mg/day.
- Current use of tramadol.
- Prior participation in psilocybin-assisted therapy trial and or regular use of hallucinogens
- Treatment with another investigational drug or other intervention during study period.

Ages Eligible for Study

18 Years to 70 Years (Adult, Older Adult)

Sexes Eligible for Study

All

Accepts Healthy Volunteers

No

Study Plan

This section provides details of the study plan, including how the study is designed and what the study is measuring.

How is the study designed?

Design Details

Primary Purpose : Treatment
Allocation : Randomized
Interventional Model : Parallel Assignment
Interventional Model Description: Participants are randomized into one of two groups and will receive either one single treatment of psilocybin-assisted therapy with follow-up therapy and assessments or two treatments spaced two weeks apart with follow-up therapy and assessments.
Masking : Single (Outcomes Assessor)
Masking Description: Due to the nature of the study and limitations of study staffing, only those conducting assessments and ratings throughout the study will be masked to the treatments. All others, including participants, therapists, investigators, and study coordinator, will not be masked to the number of treatments a participant receives.

Arms and Interventions

Participant Group/Arm	Intervention/Treatment
Experimental: Single Psilocybin Treatment Participants will be administered one dose of a 25mg capsule of psilocybin. This will be administered one time.	Drug: psilocybin • 25mg of psilocybin administered during treatment session, accompanied by preparation before, integration after, and assistive therapy during the session.
Active Comparator: Two Psilocybin Treatments Participants will be administered one dose of a 25mg capsule of psilocybin. Two weeks later, the participant will be administered one more dose of a 25mg capsule of psilocybin.	Drug: psilocybin • 25mg of psilocybin administered during treatment session, accompanied by preparation before, integration after, and assistive therapy during the session.

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Change in HAM-D-17 Scores between	The change in Hamilton Depression Rating Scale 17 item (HAM-D-17) scores between baseline and 2 weeks after treatment	Baseline, 2 weeks

Baseline and 2 Weeks after Treatment	The HAM-D-17 is a 17-item questionnaire used to measure severity of depression. The score ranges from 0 to 52. Higher scores indicate more severe depression.	
Change in QIDS SR-16 Scores between Baseline and 2 Weeks after Treatment	The change between depression scores as reported by Quick Inventory of Depressive Symptomatology Short Response-16 (QIDS SR-16) scores between baseline and 2 weeks after treatment The QIDS SR-16 is a 16-item questionnaire used to measure severity of depression. The scores range from 0 to 45. Higher scores indicate more severe depression.	Baseline, 2 weeks
Number of Participants Achieving Remission 2 Weeks after Treatment	Number of participants achieving remission (defined as a HAM-D-17 score less than 10) 2 weeks after treatment	up to 2 weeks
Number of Participants Achieving Response 2 weeks after treatment	Number of participants achieving response (defined as a HAM-D-17 score that has decreased by greater than or equal to 50 percent compared to baseline) 2 weeks after treatment	up to 2 weeks

Secondary Outcome Measures

Outcome Measure	Measure Description	Time Frame

Number of Participants Achieving Remission at 6 Weeks	Number of participants achieving remission (defined as a HAM-D-17 score less than 10) 6 weeks after treatment	up to 6 weeks
Number of Participants Achieving Response at 6 Weeks	Estimate the number of participants achieving response (defined as a HAM-D-17 score that has decreased by greater than or equal to 50 percent compared to baseline) at 6 weeks after treatment	up to 6 weeks
Number of Participants Achieving Remission at 3 Months	Number of participants achieving remission (defined as a HAM-D-17 score less than 10) 3 months after treatment	up to 3 months
Number of Participants Achieving Response at 3 Months	Estimate the number of participants achieving response (defined as a HAM-D-17 score that has decreased by greater than or equal to 50 percent compared to baseline) at 3 months after treatment	up to 3 months
Number of Participants Achieving Remission at 6 Months	Number of participants achieving remission (defined as a HAM-D-17 score less than 10) 6 months after treatment	up to 6 months
Number of Participants Achieving Response at 6 Months	Estimate the number of participants achieving response (defined as a HAM-D-17 score that has decreased by greater than or equal to 50 percent compared to baseline) at 6 months after treatment	up to 6 months

Number of Participants Achieving Remission at 9 Months	Number of participants achieving remission (defined as a HAM-D-17 score less than 10) 9 months after treatment	up to 9 months
Number of Participants Achieving Response at 9 Months	Estimate the number of participants achieving response (defined as a HAM-D-17 score that has decreased by greater than or equal to 50 percent compared to baseline) at 9 months after treatment	up to 9 months
Number of Participants Achieving Remission at 12 Months	Number of participants achieving remission (defined as a HAM-D-17 score less than 10) 12 months after treatment	up to 12 months
Number of Participants Achieving Response at 12 Months	Estimate the number of participants achieving response (defined as a HAM-D-17 score that has decreased by greater than or equal to 50 percent compared to baseline) at 12 months after treatment	up to 12 months
Time to Relapse in Participants Who Showed Remission at 2 weeks	Of the number of participants achieving remission (defined as a HAM-D-17 score less than 10) 2 weeks after treatment, the amount of time until a relapse occurring thereafter occurs. Relapse is defined as a HAM-D-17 score greater than or equal to 17 and will be measured up to the study follow-up visit at 1 year.	up to 1 year after treatment

Time to Relapse in Participants Who Showed Response at 2 Weeks	Of the number of participants achieving remission (defined as a HAM-D-17 score that has decreased by greater than or equal to 50 percent compared to baseline) 2 weeks after treatment, the amount of time until a relapse occurring thereafter occurs. Relapse is defined as a HAM-D-17 score greater than or equal to 17 and will be measured up to the study follow-up visit at 1 year.	up to 1 year after treatment
Change in HAM-D-17 Scores between Baseline and 6 Weeks after Treatment	The change in HAM-D-17 scores between baseline and 2 weeks after treatment The HAM-D-17 is a 17-item questionnaire used to measure severity of depression. The score ranges from 0 to 52. Higher scores indicate more severe depression.	Baseline, 6 weeks
Change in HAM-D-17 Scores between Baseline and 3 Months after Treatment	The change in HAM-D-17 scores between baseline and 2 weeks after treatment The HAM-D-17 is a 17-item questionnaire used to measure severity of depression. The score ranges from 0 to 52. Higher scores indicate more severe depression.	Baseline, 3 Months
Change in HAM-D-17 Scores between Baseline and 6	The change in HAM-D-17 scores between baseline and 2 weeks after treatment The HAM-D-17 is a 17-item questionnaire used to measure severity of depression. The	Baseline, 6 Months

Months after Treatment	score ranges from 0 to 52. Higher scores indicate more severe depression.	
Change in HAM-D-17 Scores between Baseline and 9 Months after Treatment	The change in HAM-D-17 scores between baseline and 2 weeks after treatment The HAM-D-17 is a 17-item questionnaire used to measure severity of depression. The score ranges from 0 to 52. Higher scores indicate more severe depression.	Baseline, 9 Months
Change in HAM-D-17 Scores between Baseline and 12 Months after Treatment	The change in HAM-D-17 scores between baseline and 2 weeks after treatment The HAM-D-17 is a 17-item questionnaire used to measure severity of depression. The score ranges from 0 to 52. Higher scores indicate more severe depression.	Baseline, 12 months
Change in QIDS SR-16 Scores between Baseline and 6 Weeks after Treatment	The change between depression scores as reported by QIDS SR-16 scores between baseline and 2 weeks after treatment The QIDS SR-16 is a 16-item questionnaire used to measure severity of depression. The scores range from 0 to 45. Higher scores indicate more severe depression.	Baseline, 6 weeks

Change in QIDS SR-16 Scores between Baseline and 3 Months after Treatment	The change between depression scores as reported by QIDS SR-16 scores between baseline and 2 weeks after treatment The QIDS SR-16 is a 16-item questionnaire used to measure severity of depression. The scores range from 0 to 45. Higher scores indicate more severe depression.	Baseline, 3 Months
Change in QIDS SR-16 Scores between Baseline and 6 Months after Treatment	The change between depression scores as reported by QIDS SR-16 scores between baseline and 2 weeks after treatment The QIDS SR-16 is a 16-item questionnaire used to measure severity of depression. The scores range from 0 to 45. Higher scores indicate more severe depression.	Baseline, 6 Months
Change in QIDS SR-16 Scores between Baseline and 9 Months after Treatment	The change between depression scores as reported by QIDS SR-16 scores between baseline and 2 weeks after treatment The QIDS SR-16 is a 16-item questionnaire used to measure severity of depression. The scores range from 0 to 45. Higher scores indicate more severe depression.	Baseline, 9 Months
Change in QIDS SR-16 Scores between Baseline and 12 Months after Treatment	The change between depression scores as reported by QIDS SR-16 scores between baseline and 2 weeks after treatment The QIDS SR-16 is a 16-item questionnaire used to measure severity of depression. The	Baseline, 12 Months

	scores range from 0 to 45. Higher scores indicate more severe depression.	

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor

University of North Carolina, Chapel Hill

Collaborators

- Foundation of Hope, North Carolina

Investigators

- Principal Investigator: Robert K McClure, MD, Director of Interventional Psychiatry

Publications

General

These publications are provided voluntarily by the person who enters information about the study and may be about anything related to the study.

- Demyttenaere K, Van Duppen Z. The Impact of (the Concept of) Treatment-Resistant Depression: An Opinion Review. Int J Neuropsychopharmacol. 2019 Feb 1;22(2):85-92. doi: 10.1093/ijnp/pyy052. (https://pubmed.ncbi.nlm.nih.gov/29961822)
- Dold M, Kasper S. Evidence-based pharmacotherapy of treatment-resistant unipolar depression. Int J Psychiatry Clin Pract. 2017 Mar;21(1):13-23. doi: 10.1080/13651501.2016.1248852. Epub 2016 Nov 16. (https://pubmed.ncbi.nlm.nih.gov/27848269)
- Ross S, Bossis A, Guss J, Agin-Liebes G, Malone T, Cohen B, Mennenga SE, Belser A, Kalliontzi K, Babb J, Su Z, Corby P, Schmidt BL. Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial. J Psychopharmacol. 2016 Dec;30(12):1165-1180. doi: 10.1177/0269881116675512. (https://pubmed.ncbi.nlm.nih.gov/27909164)

- Rush AJ, Trivedi MH, Wisniewski SR, Nierenberg AA, Stewart JW, Warden D, Niederehe G, Thase ME, Lavori PW, Lebowitz BD, McGrath PJ, Rosenbaum JF, Sackeim HA, Kupfer DJ, Luther J, Fava M. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. Am J Psychiatry. 2006 Nov;163(11):1905-17. doi: 10.1176/ajp.2006.163.11.1905. (https://pubmed.ncbi.nlm.nih.gov/17074942)

- Keller MB, Shapiro RW, Lavori PW, Wolfe N. Recovery in major depressive disorder: analysis with the life table and regression models. Arch Gen Psychiatry. 1982 Aug;39(8):905-10. doi: 10.1001/archpsyc.1982.04290080025004. (https://pubmed.ncbi.nlm.nih.gov/7103679)

- Griffiths RR, Johnson MW, Carducci MA, Umbricht A, Richards WA, Richards BD, Cosimano MP, Klinedinst MA. Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. J Psychopharmacol. 2016 Dec;30(12):1181-1197. doi: 10.1177/0269881116675513. (https://pubmed.ncbi.nlm.nih.gov/27909165)

- Carhart-Harris R, Giribaldi B, Watts R, Baker-Jones M, Murphy-Beiner A, Murphy R, Martell J, Blemings A, Erritzoe D, Nutt DJ. Trial of Psilocybin versus Escitalopram for Depression. N Engl J Med. 2021 Apr 15;384(15):1402-1411. doi: 10.1056/NEJMoa2032994. (https://pubmed.ncbi.nlm.nih.gov/33852780)

- Carhart-Harris RL, Bolstridge M, Rucker J, Day CM, Erritzoe D, Kaelen M, Bloomfield M, Rickard JA, Forbes B, Feilding A, Taylor D, Pilling S, Curran VH, Nutt DJ. Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study. Lancet Psychiatry. 2016 Jul;3(7):619-27. doi: 10.1016/S2215-0366(16)30065-7. Epub 2016 May 17. (https://pubmed.ncbi.nlm.nih.gov/27210031)

- Carhart-Harris RL, Bolstridge M, Day CMJ, Rucker J, Watts R, Erritzoe DE, Kaelen M, Giribaldi B, Bloomfield M, Pilling S, Rickard JA, Forbes B, Feilding A, Taylor D, Curran HV, Nutt DJ. Psilocybin with psychological support for treatment-resistant depression: six-month follow-up. Psychopharmacology (Berl). 2018 Feb;235(2):399-408. doi: 10.1007/s00213-017-4771-x. Epub 2017 Nov 8. (https://pubmed.ncbi.nlm.nih.gov/29119217)

- Davis AK, Barrett FS, May DG, Cosimano MP, Sepeda ND, Johnson MW, Finan PH, Griffiths RR. Effects of Psilocybin-Assisted Therapy on Major Depressive Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2021 May 1;78(5):481-489. doi: 10.1001/jamapsychiatry.2020.3285. Erratum In: JAMA Psychiatry. 2021 Feb 10:569. doi: 10.1001/jamapsychiatry.2020.4714. (https://pubmed.ncbi.nlm.nih.gov/33146667)

- Gukasyan N, Davis AK, Barrett FS, Cosimano MP, Sepeda ND, Johnson MW, Griffiths RR. Efficacy and safety of psilocybin-assisted treatment for major depressive disorder: Prospective 12-month follow-up. J Psychopharmacol. 2022 Feb;36(2):151-158. doi: 10.1177/02698811211073759. (https://pubmed.ncbi.nlm.nih.gov/35166158)

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- Maclean KA, Leoutsakos JM, Johnson MW, Griffiths RR. Factor Analysis of the Mystical Experience Questionnaire: A Study of Experiences Occasioned by the Hallucinogen Psilocybin. J Sci Study Relig. 2012 Dec;51(4):721-737. doi: 10.1111/j.1468-5906.2012.01685.x. (https://pubmed.ncbi.nlm.nih.gov/23316089)

- Murphy R, Kettner H, Zeifman R, Giribaldi B, Kartner L, Martell J, Read T, Murphy-Beiner A, Baker-Jones M, Nutt D, Erritzoe D, Watts R, Carhart-Harris R. Therapeutic Alliance and Rapport Modulate Responses to Psilocybin Assisted Therapy for Depression. Front Pharmacol. 2022 Mar 31;12:788155. doi: 10.3389/fphar.2021.788155. eCollection 2021. (https://pubmed.ncbi.nlm.nih.gov/35431912)

- Bond FW, Hayes SC, Baer RA, Carpenter KM, Guenole N, Orcutt HK, Waltz T, Zettle RD. Preliminary psychometric properties of the Acceptance and Action Questionnaire-II: a revised measure of psychological inflexibility and experiential avoidance. Behav Ther. 2011 Dec;42(4):676-88. doi: 10.1016/j.beth.2011.03.007. Epub 2011 May 25. (https://pubmed.ncbi.nlm.nih.gov/22035996)

Study Record Dates

These dates track the progress of study record and summary results submissions to ClinicalTrials.gov. Study records and reported results are reviewed by the National Library of Medicine (NLM) to make sure they meet specific quality control standards before being posted on the public website.

Study Registration Dates

First Submitted
2024-02-27

First Submitted that Met QC Criteria
2024-03-04

First Posted
2024-03-12

Study Record Updates

Last Update Submitted that met QC Criteria
2024-07-19

Last Update Posted

2024-07-23

Last Verified

2024-07

More Information

Terms related to this study

Keywords Provided by University of North Carolina, Chapel Hill

psilocybin
psychedelic
refractory depression
psychedelic-assisted therapy
treatment-resistant depression
TRD
depression

Additional Relevant MeSH Terms

Behavioral Symptoms
Mood Disorders
Mental Disorders
Depression
Depressive Disorder
Depressive Disorder, Treatment-Resistant
Hallucinogens
Physiological Effects of Drugs
Psychotropic Drugs
Psilocybin

Plan for Individual Participant Data (IPD)

Plan to Share Individual Participant Data (IPD)?

Yes

IPD Plan Description

Deidentified individual data that supports the results will be shared beginning 9 to 36 months following publication provided the investigator who proposes to use the data has approval from an Institutional Review Board (IRB), Independent Ethics Committee (IEC), or Research Ethics Board (REB), as applicable, and executes a data use/sharing agreement with UNC.

IPD Sharing Access Criteria

Investigator has approved IRB, IEC, or REB and an executed data use/sharing agreement with UNC.

IPD Sharing Time Frame

Data will be provided beginning 9 and continuing for 36 months following publication.

IPD Sharing Supporting Information Type

Study Protocol
Statistical Analysis Plan (SAP)
Informed Consent Form (ICF)

Drug and device information, study documents, and helpful links

Studies a U.S. FDA-Regulated Drug Product

Yes

Studies a U.S. FDA-Regulated Device Product

No